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The Huriez syndrome. Scleroatrophic palmoplantar keratoderma

We describe a mother and son exhibiting a rare subtype of palmoplantar keratoderma, characterized by scleroatrophy, sclerodactyly, and nail anomalies. In the affected skin of the mother, 3 squamous cell carcinomas had developed at a young age. Retinoid treatment was started prophylactically. After the original description by Huriez *et al.* in 1963, six other families and one case report have been described. The palmoplantar keratoderma is usually mild. However, the distinctive feature of this syndrome is malignant degeneration of the affected skin at a young age. Furthermore, an unusually high mortality rate for this type of skin cancer of 5% has been reported. This case is described in order to underline the importance of accurate specification of each hereditary palmoplantar keratoderma. The characteristic clinical hallmarks of Huriez syndrome enable a rapid diagnosis, which is important for preventing malignant degeneration. Prophylaxis by retinoid treatment is discussed. *(Key words: keratoderma, palmoplantar, Huriez, sclerodactyly, malignant degeneration.)*

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In 1963, Huriez *et al.* [1-3] described an autosomal, dominantly inherited syndrome, characterized by a diffuse palmoplantar keratoderma with sclerodactyly and nail changes, in two families resident in the north of France. The palmoplantar keratoderma consists of a discrete, sometimes lamellated hyperkeratosis with atrophy, diffusely covering, in particular, the palmar skin. The plantar skin usually displays less severe involvement. Atrophic plaques may be found on the dorsa of the hands and fingers. Obligatorily associated features are sclerodactyly and nail changes. The sclerodactyly strongly resembles scleroderma, although the genetic inheritance, absence of systemic symptoms, lack of vasomotor phenomena, appearance of the initial symptoms at birth or in early childhood, and absence of progression during adulthood, enable a differentiation. Nail changes consist of aplasia, ridging and clubbing. Hypohidrosis is associated in half of the cases. The disease usually starts at birth or during early childhood and persists unchanged throughout adult life. The distinctive feature of this syndrome is the risk of the development of squamous cell carcinoma on the affected skin, which may occur as early as the third or fourth decade. Until now, seven families [1-8] and one case report [9] have been published. We describe another family affected with Huriez syndrome.

Case report

A 34-year-old woman presented with a palmoplantar keratoderma, focally involving the dorsal surfaces, that had appeared at the age of 1 year. At the age of 31, four hyperkeratotic nodules and plaques had developed progressively on the affected skin on the dorsal side of the left hand. After surgical removal, histopathological examination revealed squamous cell carcinoma in three of them.

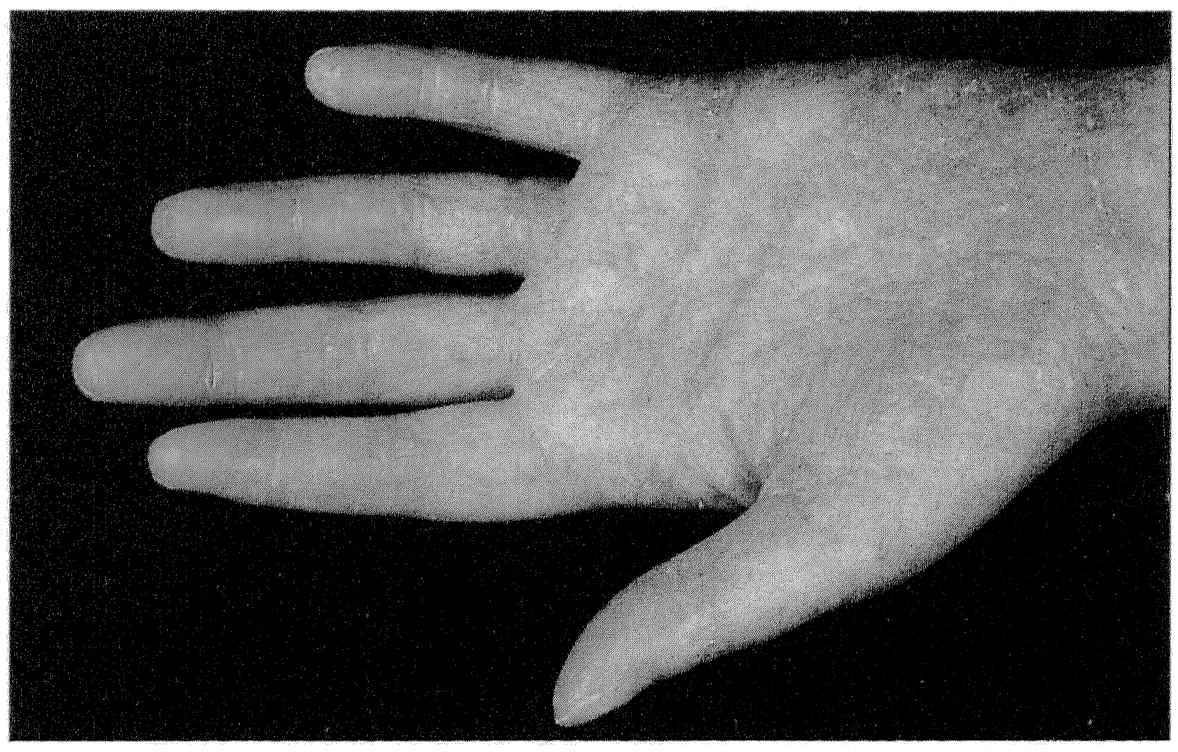

Figure 1. *Palmar skin of the mother, showing a diffuse, thin hyperkeratosis with erythema and atrophy. Dermatoglyphic patterns are lost. Extension of the fingers is limited due to sclerodactyly.*

Similar, though less pronounced palmoplantar hyperkeratosis, had appeared shortly after birth in her son. Up until then there had been no family history of any similar lesions. The maternal family history revealed that ancestors had lived in the north of France.
Examination of the mother revealed thin hyperkeratoses with erythema and atrophy on the palmoplantar skin, with small areas of normal skin in between. Focally, a prokeratotic appearance was observed, whereas the dermatoglyphic pattern was abnormal *(Fig. 1)*. The palmar lesions were restricted to the palms, and did not spread to the dorsal

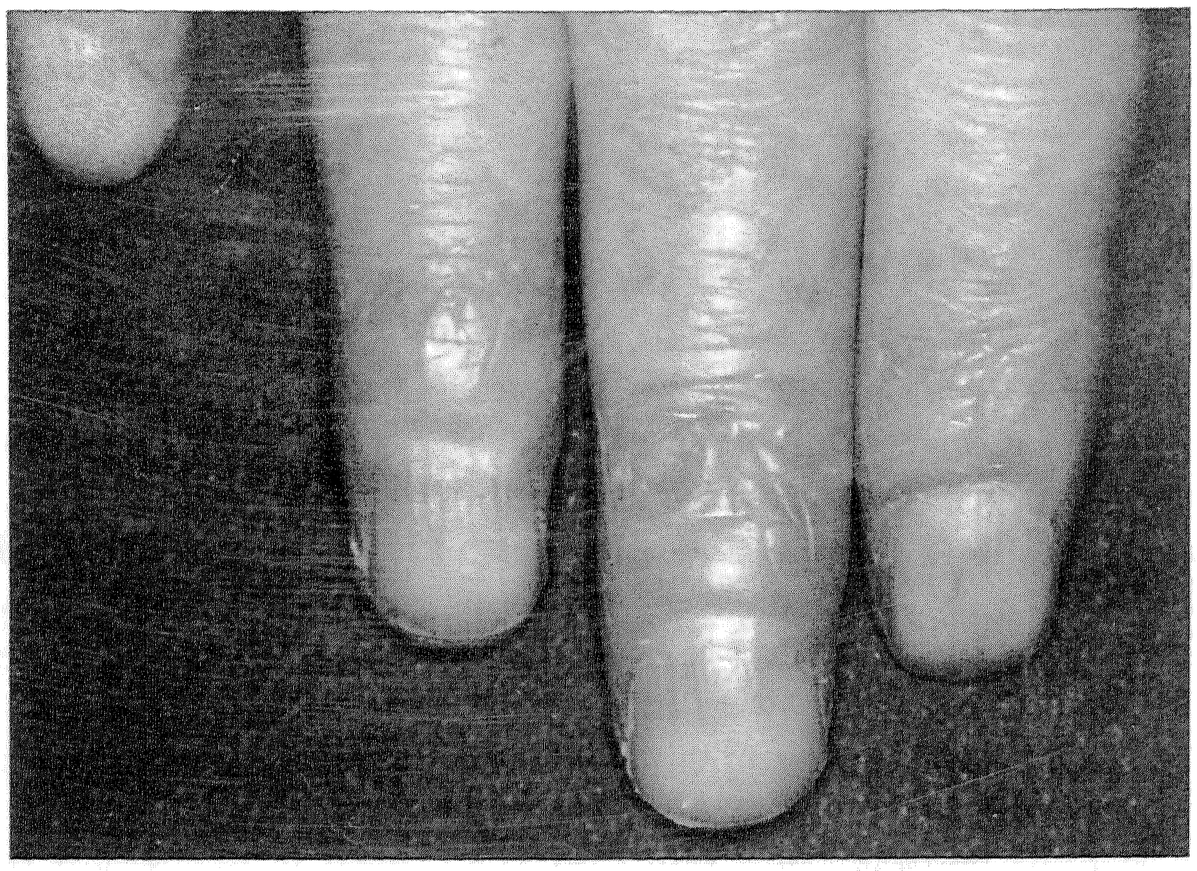

Figure 2. *Sclerosis of the skin of all fingers. The fingernails display ridging.*

skin. In addition, irregular areas with similar lesions were observed on the dorsal skin of the hands. The dorsal skin of the feet displayed no abnormalities. All fingers of both hands revealed a marked sclerosis of the skin *(Fig. 2)*. Most fingernails showed longitudinal ridging. Examination of her son revealed palmar erythema with slight, hyperkeratotic desquamation. Erythematous, slightly hyperkeratotic plaques were observed on the dorsal skin overlying the finger joints of the hands *(Fig. 3)*. Sclerodactyly prevented full extension of the fingers. Cheilitis was not observed in either patients.

Histopathological examination of the palmar skin of the mother demonstrated hyperkeratosis, acanthosis and papillomatosis. Epidermolytic hyperkeratosis was absent. Therapy was started with calcipotriol ointment once daily on the right palmar and plantar skin. After 5 weeks of therapy, no beneficial effect was observed. The application frequency of calcipotriol was doubled. In addition, oral acitretin treatment was started with a daily dose of 25 mg. Mucocutaneous retinoid side effects were observed although they were not severe, and were well tolerated. After 2 months of treatment, a slight reduction of the hyperkeratosis was observed. There was no left-right difference.

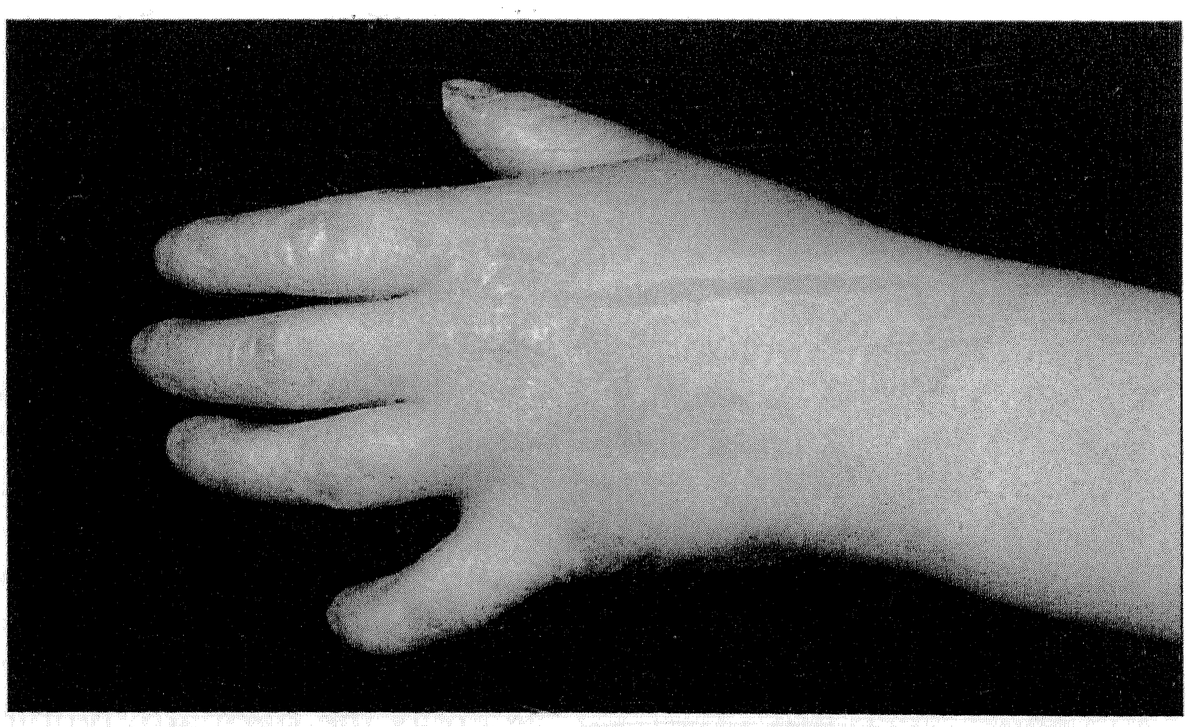

Figure 3. *Atrophic, erythematous, slightly keratotic plaques covering the dorsal skin of the finger joints in the son.*

Discussion

We have described a mother and son with Huriez syndrome. The mother developed three squamous cell carcinomas in the affected dorsal skin of the left hand. Possibly, ancestors of this family and the families described by Huriez, both resident in the North of France, were common.

Until now seven families and one sporadic case have been described, including the original description by Huriez *et al.* [1-9]. Malignant degeneration of the affected skin was observed in 11/86 affected family members (average 13%). Four of them had died from metastasis of their cutaneous malignancy. This unusually high mortality rate of 5% might be explained by the frequently low grade of differentiation. As several affected family members described were often young, the lifetime risk is probably even higher. Hamm *et al.* [8] found a virtual absence of epidermal Langerhans cells in the involved skin. The resulting diminution of recognition and presentation of tumour-associated antigens, might contribute to the tendancy to malignant degeneration.

Yesudian *et al.* [10] described a family with palmoplantar keratoderma clinically identical to that observed in Huriez syndrome. In 3/22 tylotic family members, squamous cell carcinomas were found in the affected skin, and one died of squamous cell carcinoma of the oesophagus. A similar association with internal malignancies has not been described in other patients. Malignant degeneration of the tylotic skin has also been observed in Schöpf-Schulz-Passarge syndrome, which can be differentiated easily from Huriez syndrome [11]. No other palmoplantar keratodermas are known to be associated with the development of squamous cell carcinomas of affected skin.

The enhanced risk of the development of squamous cell carcinoma on the affected skin at a young age, in Huriez syndrome, underlines the statement that the accurate specification and diagnosis of an individual patient presenting with a hereditary palmoplantar keratoderma is not an academic exercise but is extremely important for individual patient management to allow optimal treatment and follow-up in those at risk of skin cancer. As we have described recently, specific morphology and distribution of the hyperkeratosis, the inheritance pattern and the presence or absence of associated features, are the most important features enabling a rapid classification. Additional criteria are the presence of skin lesions on areas other than the palms and soles, the age of onset of the keratoderma, the severity of the disease process and the histological findings [12]. Concerning treatment of Huriez syndrome, almost no data are available. Retinoids have been used succesfully in several other types of palmoplantar keratoderma [13-17]. Furthermore, there is increasing evidence that retinoids are effective as prophylaxis against the development of neoplasias of the skin [18, 19]. Until now, only one patient with the Huriez syndrome had been treated with retinoids for more than 5 years. This patient did not develop any further squamous cell carcinomas during this period [20].

In conclusion, patients with Huriez syndrome should be regarded as at risk for the development of squamous cell carcinomas on the affected skin. Therefore, regular follow-up and a full explanation to the patient are essential. Treatment with retinoids might be considered. ■

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